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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/147,693	02/17/1999	WERNER LUBITZ	P564-9005	2068

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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	30

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/147,693	Applicant(s) Lubitz et al.
	Examiner William Sandals	Art Unit 1636

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Feb 28, 2003*

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-45, 49-65, 69-72, 77, and 78* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5)☒ Claim(s) *38-45, 49-62, 69, 70, 77, and 78* is/are allowed.

6)☒ Claim(s) *63-65, 71, and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 38-45, 49-65, 69-72 and 77-78 are pending. Claims 46, 48 and 73-76 have been cancelled by amendment in Paper No. 28, filed February 28, 2003.

2. Claims 63-65 and 71-72 stand rejected under 35 U.S.C. 112, first paragraph. Response to arguments follows the rejection.

Response to Arguments

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 63-65 and 71-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a vaccine. Vaccine making is a poorly enabled art which relies heavily on a trial and error process for discovery and development. The instant claims drawn to a vaccine do not provide the necessary information for the making of a vaccine to an unspecified antigen, since vaccine production is an art which relies upon specific experimentation with each potential antigen in order to prove that protective immunity can be produced. In order to do so, undue experimentation is required. Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors. Many of these factors have been summarized in *In re Wands*, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).

The Wands factors as they apply to the instant claimed invention are as follows:

a- The quantity of experimentation necessary to reduce the instant claimed invention to practice would involve a trial and error process for testing and evaluating any prospective preparation for its' activity as a vaccine.

b- Only prophetic guidance is provided in the manufacture of a vaccine. No working examples of a vaccine have been provided in the instant specification.

c- The nature of the invention is complex. Vaccine making is a poorly understood art.

d- The state of the art of vaccine making is one of uncertainties, as stated by Miller (Curr. Opinion in Infectious Dis. Vol. 10:183-187, 1997). Miller states at the conclusion "[s]ignificant advances have been made in the past year. Several safe and effective adjuvants that may be useful in human vaccines have been identified. In addition, many recent studies have revealed that oral immunization with bacterial endotoxin/antigen preparations, recombinant attenuated

vaccine strains, or naked DNA-based vaccines can elicit potent systemic and mucosal responses that sometimes confer protective immunity. The results offer hope that safe, effective, easily administered and relatively inexpensive vaccines against a variety of human pathogens are on the horizon." The message is clear that one year post-filing of the instant claimed invention, that vaccine production still was unreliable and unpredictable.

e- Those of skill in the art of vaccine making are presented with many problems which do not have clear and certain answers, as discussed by Gregoriadis (Pharm Res. Vol. 15(5):661-670, 1998). Gregoriadis emphasizes the difficulties of making vaccines with killed microbes, because limited knowledge of how to induce an immune response which will confer systemic immunity continues to the present day to perplex those of skill in the art. It is noted that antibody production is possible, but concomitant systemic immunity may, or may not, be produced. Gregoriadis proposes future hopes for vaccine production in alternatives such as recombinant DNA vaccines.

f- The uncertainty of making a vaccine is highlighted by Miller and by Gregoriadis, demonstrating the unpredictability of making a vaccine, and that one of skill in the art does not know how to predictably make a vaccine.

g- The breadth of the claims encompass any vaccine which is made with a bacteria. In view of the foregoing reasons, there is no support in the claims or specification for the breadth of these claims.

g- Therefore, given the analysis above, it must be considered that the skilled artisan would have needed to have practiced considerable non-routine, trial and error experimentation to enable the claimed subject matter.

5. Arguments presented in Paper No. 28, page 5, assert that the specification teaches at pages 8-11 how to make and use bacterial ghosts as vaccines, and at pages 10-11 list several suitable cells for making vaccines. It is asserted that previously submitted references, as well as a reference by Panthel et al. submitted in Paper No. 28 teach the enablement of bacterial ghosts as vaccines.

The discussion section in Panthel et al. restates the lack of knowledge as to why the reported success of reduction in intestinal H. pylori bacteria following challenge with H. pylori ghosts occurred. To emphasize this message, at page 113 column 2, bottom, bridging to page 114, column 2, top, Panthel et al. teach that attempts to immunize with killed bacterial preparations were unsuccessful, and speculates on possible reasons for this lack of success.

As stated in the rejection above, merely setting forth some general guidelines for using the claimed invention as taught in the instant specification, does not overcome the problems of uncertainty of vaccine production in general. Each potential vaccine must be experimentally proven by a trial and error process. Therefore, the arguments are not found convincing.

Allowable Subject Matter

6. Claims 38-45 and 49-62, 69, 70, 77 and 78 are allowed.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.
Examiner
May 30, 2003

REMY YUCEL, PH.D
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